DETAILED ACTION

Claims and Previous Rejections/Objections Status

1. Claims 2-4,6-139,141 and 143-145 are pending in the application. Claims 42-139 are withdrawn from consideration. Claims 144 and 145 were amended in the response filed 3/15/11. Support for this amendment was found in the specification, p35, lines 24+ and figures 2A and 2B.

2. The rejection of claims 2,6,11,13-18,20-25,27-31,36-39 and 143-145 under 35 U.S.C. 103(a) as being unpatentable over by Rossling et al. (US 6,468,506B1) is maintained.

3. The rejection of claims 2-4,6-41,141 and 143-145 under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Uber, III et al. (US 6,397,098) and in further view of Quay et al. (WO 96/40282) or in further view of Daum et al. (US 6,231,513) and Engel (EP0135822) is maintained.

Response to Arguments

4. Applicant's arguments filed 3/15/11 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 2,6,11,13-18,20-25,27-31,36-39 and 143-145 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) as stated in the action mailed 11/9/10.

7. Claims 2-4,6-41,141 and 143-145 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Uber, III et al. (US 6,397,098) and in further view of Quay et al. (WO 96/40282) or in further view of Daum et al. (US 6,231,513) and Engel (EP0135822) as stated in the action mailed 11/9/10.

8. Applicant asserts that neither alone nor in combination do the prior art references teach "a system for preparing a medium with bubbles formed therein for immediate injection into a patient...." of the type claimed in the independent claims. In particular, individually or collectively, the prior art fails to disclose such a system having a "controller [that] enables an operator of said system to adjust at least one operating parameter thereof through which to control simultaneously (I) the pressurizing device and flow of the liquid therefrom into the bubble generator, (II) the bubble generator and creation of the bubbles in the liquid to form the medium therein and (III) flow of the medium from the bubble generator via the outlet thereof thus allowing the immediate injection of the medium into the patient in connection with the medical procedure."

9. The reference of Rossling et al. was not explicitly used to teach of a controller. The reference of Rossling et al. was used to teach of a system/apparatus for the production of gaseous microparticles/plurality of differentiable populations of bubbles/bubble medium for ultrasound diagnosis (i.e.

imaging procedure) and the process for the production of gaseous microparticles. The apparatus comprises a tank **(17)** (i.e. reservoir for storing a liquid) which may be filled with gas via a valve **(2)**, line/gas flow path **(30)** and a pump **(16**) and/or liquid gas pump **(4)**. The bubble generator, having an inlet and outlet, used to create gaseous microparticles involves pumping in gas into a surface-active substance solution, applying a vacuum and mixing with a stirring mechanism (i.e. means for disrupting an interface) between the liquid and the gas, not excluding multiple small wires or disks.

10. At the time of the invention it would have been obvious to one ordinarily skilled in the art that the controller may be a scientist that can manually change operating parameters, such as controlling the pressurizing device and flow of liquid, creation of the bubbles in liquid to form the medium and flow of the medium from the generator via the outlet and thus the system/apparatus of the disclosure does not exclude a controller.

11. The system/apparatus and controller of Rossling et al. encompass the bubble generator and controller components of the instant claims, such as an outlet for conveying the medium immediately after formation of the bubbles therein to the patient for immediate injection therein and are capable of the same functions as the bubble generator and controller of the instant claims.

12. Applicant asserts that, as explained in earlier arguments, incorporated herein by reference, the Rossling et al. patent teaches only a process of producing pre-packaged (dried, spherically-shaped, gas-containing) microparticles to which water can be added later to form a bubble contrast

medium. The Uber, III et al. patent teaches the filling of a syringe with such a pre-made medium and then placing it into their injector system. After the syringe containing the rehydrated bubble medium is loaded into the system of Uber et al., its combination with the teachings of Rossling et al. yield the same system as that taught in the Uber, III et al. patent itself, specifically, a system that is only capable of reducing the concentration of bubbles in the medium to a desired level. Quay et al. pertains only to bulk formation of a bubble contrast medium, which is then injected into the blood stream. Daum et al. pertains only to creation of bubbles directly within a blood vessel by means of gas injected via a needle. Neither reference discloses a controller that permits an operator to adjust the operating parameters of the system through which to control, for example, not only the bubble generator but also the creation of the bubble medium therein and the flow of the medium therefrom immediately into the patient. This is something that the prior art simply does not do.

13. The reference of Rossling et al. was not explicitly used to teach of a controller. The reference of Rossling et al. was used to teach of a system/apparatus for the production of gaseous microparticles/plurality of differentiable populations of bubbles/bubble medium for ultrasound diagnosis (i.e. imaging procedure) and the process for the production of gaseous microparticles. The apparatus comprises a tank **(17)** (i.e. reservoir for storing a liquid) which may be filled with gas via a valve **(2)**, line/gas flow path **(30)** and a pump **(16**) and/or liquid gas pump **(4)**. The bubble generator, having an inlet and outlet, used to create gaseous microparticles involves pumping in gas into a surface-active

substance solution, applying a vacuum and mixing with a stirring mechanism (i.e. means for disrupting an interface) between the liquid and the gas, not excluding multiple small wires or disks

14. The system/apparatus and controller of Rossling et al. encompass the bubble generator and controller components of the instant claims, such as an outlet for conveying the medium immediately after formation of the bubbles therein to the patient for immediate injection therein and are capable of the same functions as the bubble generator and controller of the instant claims.

15. The references of Uber, III et al., Quay et al., Daum et al. and Engel were not used to teach of a controller.

16. The reference of Uber, III et al. was used to teach of a system for producing a contrast-enhanced medical image of a patient comprising a concentration regulator (i.e. verification device) which selectively destroys microbubbles and an imaging unit to provide (preferably in real-time) an indication (for example, a visual or audible indication) of an internal state, condition or view of the patient based upon a signal resulting from the energy applied to the region of a patient. The system involves the injection of a contrast or enhancement medium and may be used in connection with general components or pieces of equipment manufactured by more than one company, not excluding the system for generating microbubbles of Rossling et al.

17. At the time of the invention it would have been obvious to one ordinarily skilled in the art to create gaseous microparticles with the apparatus of Rossling et al. and administer them to a patient with the injector system of Uber, III et al.

for direct administration of the contrast agent to a patient as Uber, III et al. teaches that the pressurizing unit of the system (Uber, III et al.) is in fluid connection with the source of fluid medium (contrast or enhancement medium) to pressurize the fluid medium for the advantage of direct injection into the patient. The outlet of Rossling et al. encompasses the outlet of the instant claims and allows for conveying the medium immediately after formation of the bubbles therein. Uber, III et al. also teaches that the system may include general components or pieces of equipment manufactured by more than one company (Uber, III et al. column 2, lines 42-45), not excluding the system for generating microbubbles of Rossling et al.

18. The reference of Quay et al. was used to teach of the enhanced production of gaseous microbubbles via the introduction of solid particles in the gas-liquid emulsion where there is a significant increase in bubble population per unit volume.

19. The reference of Daum et al. was used to teach of a microbubble forming arrangement having a plurality of microholes which when a gas is passed through causes the gas to form numerous microbubbles in fluid and the use of piezoelectric ultrasound for the preparation of gas-filled microbubbles used for ultrasound diagnosis.

20. The reference of Engel was used to teach of a diffusor (plate) or a series-arrangement for the throughpassage of a fluid having a multitude of channels which extend therethrough in a mutually parallel relationship (abstract). The

diffuser enables a particularly uniform distribution of the fluid over large surface areas (p1, lines 24-28) and the generation of a stream of fine bubbles.

21. At the time of the invention it would have been obvious to one ordinarily skilled in the art to generate microparticles via nucleation with solid particles as it is a known technique in the art for generating gaseous microparticles with significant increase in bubble population per unit volume and thus provides enhanced imaging.

22. At the time of the invention it would have been obvious to one ordinarily skilled in the art to generate microparticles via piezoelectric ultrasound or induction plate as they are known techniques in the art for generating gaseous microparticles with significant increase in bubble population per unit volume and thus provides enhanced imaging.

Conclusion

23. No claims are allowed at this time.

24. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 7-4 M, 7-4 T, 6 Th, 7-4 F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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